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## PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT  
(PCT Article 36 and Rule 70)

REC'D 23 FEB 2005

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Applicant's or agent's file reference PRD2006f-PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEAA/16)	
International application No. PCT/EP 03/50641	International filing date (day/month/year) 19.09.2003	Priority date (day/month/year) 04.11.2002
International Patent Classification (IPC) or both national classification and IPC C25B1/00		
Applicant JANSSEN PHARMACEUTICA N.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  10.04.2004	Date of completion of this report  21.02.2005
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Hammerstein, G  Telephone No. +49 89 2399-8175 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP 03/50641**

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-20 as originally filed

**Claims, Numbers**

1-15 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

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**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	1-12
	No: Claims	13-15
Inventive step (IS)	Yes: Claims	1-12
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-15
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

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**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**Novelty, Article 33 (2) PCT**

Reference is made to the following documents, in particular to those passages mentioned in the search report:

- D1: CZOLLNER L ET AL: "New Kilogram-Synthesis of the Anti-Alzheimer Drug (-)-Galanthamine" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 39, no. 15, 9 April 1998 (1998-04-09), pages 2087-2088, XP004110636 ISSN: 0040-4039
- D2: POSCHALKO A ET AL: "Synthesis of (+/-)-6H-benzofuro[3a,3,2,ef][3]benzazepine: an unnatural analog of (-)-galanthamine" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 58, no. 8, 18 February 2002 (2002-02-18), pages 1513-1518, XP004336387 ISSN: 0040-4020
- D3: US-B-6 407 2291 (JORDIS ULRICH ET AL) 18 June 2002 (2002-06-18)
- D4: DATABASE WPI Section Ch, Week 199640 Derwent Publications Ltd., London, GB; Class E31, AN 1996-400688 XP002260102 & RU 2 051 203 C (MONOMER DES INST & EXPERIM WKS) 27 December 1995 (1995-12-27)
- D5: DATABASE WPI Section Ch, Week 198751 Derwent Publications Ltd., London, GB; Class E31, AN 1987-357539 XP002260103 & HU 43 653 A (SCHREMMER I) 30 November 1987 (1987-11-30)
- D6: US-A-4 032 415 (SANDERS FREDERICK W) 28 June 1977 (1977-06-28).

The feature defined in product-by-process claim 13 reading "obtainable by a process as described in claim 1" does not restrict the claimed solutions to those actually obtained by such process.

Thus, claim 13 is not new in view of each of D1 to D6, because the documents disclose aqueous solutions comprising ferricyanide.

The subject-matter of claims 14 and 15 is not new in view of each of D1 to D3 in that the

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documents disclose the use of aqueous solutions comprising ferricyanide for an oxidative phenolic coupling reaction in order to prepare galanthamine.

The state of the art does not describe or hint to a process of oxidizing by an electrochemical reaction in a divided cell ferrocyanide (V) to ferricyanide (IV) in an aqueous solution which is recovered from an oxidative phenolic coupling reaction. The problem solved by this process is recycling of ferrocyanide solutions in phenolic coupling, in particular for the production of galanthamine.